Case # 10/525,930
AD 12/6/07
STN

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FILE 'MEDLINE' ENTERED AT 19:31:37 ON 06 DEC 2007

FILE 'BIOSIS' ENTERED AT 19:31:37 ON 06 DEC 2007
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=> s vanadate and (stem cell or progenitor cell)
L1          70 VANADATE AND (STEM CELL OR PROGENITOR CELL)

=> s culture and growth factor
L2      168201 CULTURE AND GROWTH FACTOR

=> s (culture medium) and (growth factor)
L3       28573 (CULTURE MEDIUM) AND (GROWTH FACTOR)

=> s l2 and l3
L4       28573 L2 AND L3

=> s l1 and l4
L5           1 L1 AND L4

=> disp l5 ibib abs 1-1

L5   ANSWER 1 OF 1     MEDLINE on STN
ACCESSION NUMBER:    97304299     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9160662
TITLE:               Polycythemia vera. V. Enhanced proliferation and
                     phosphorylation due to vanadate are diminished in
                     polycythemia vera erythroid progenitor
                     cells: a possible defect of phosphatase activity in
                     polycythemia vera.
AUTHOR:              Dai C H; Krantz S B; Sawyer S T
CORPORATE SOURCE:    Department of Medicine, Department of Veterans Affairs
                     Medical Center, Vanderbilt University School of Medicine,
                     Nashville, TN 37232-6305, USA.
SOURCE:              Blood, (1997 May 15) Vol. 89, No. 10, pp. 3574-81.
                     Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         199706
ENTRY DATE:          Entered STN: 30 Jun 1997
                     Last Updated on STN: 3 Mar 2000
                     Entered Medline: 19 Jun 1997
AB   Erythropoietin (EP) and stem cell factor (SCF) are
     essential growth factors for erythroid
     progenitor cell proliferation and differentiation in
     serum-free culture.  It has been previously shown that
     burst-forming units-erythroid and colony-forming units-erythroid from
     patients with polycythemia vera (PV) have enhanced sensitivity to EP and
     SCF compared with normal erythroid progenitors, but little is known about
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the mechanism for this difference. In the present investigation, the effect of EP and SCF on protein tyrosine phosphorylation in day-8 normal and PV erythroid colony-forming cells, which give rise to colonies of 2-49 hemoglobinized cells, was studied. EP rapidly induced tyrosine phosphorylation of the EP receptor, whereas the most prominent phosphorylated protein induced by SCF was identified as the SCF receptor. No additional phosphorylated proteins were evident when PV cells were compared with normal cells. Culture of normal erythroid progenitors with orthovanadate, an inhibitor of protein tyrosine phosphatases, resulted in an increased number of erythroid colonies and enhanced protein tyrosine phosphorylation. However, in contrast, little enhancement was evident with PV cells. These results indicate that, although vanadate may be acting in normal erythroid progenitors as a phosphatase inhibitor that potentiates the kinase activity induced by SCF and EP, this function is diminished in PV cells. Because erythropoiesis is regulated by a balance between protein tyrosine kinase activity and protein tyrosine phosphatase activity, PV patients may have an abnormal phosphatase activity allowing increased cell proliferation.

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=> s haggblad au
L6            0 HAGGBLAD AU

=> s haggblad and vanadate
L7            0 HAGGBLAD AND VANADATE

=> s vanadate and growth facto
L8            0 VANADATE AND GROWTH FACTO

=> s vanadate and growth factor
L9         1464 VANADATE AND GROWTH FACTOR

=> s l9 and (stem or progenitor)
L10          25 L9 AND (STEM OR PROGENITOR)

=> s l10 and culture
L11           7 L10 AND CULTURE

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12           3 DUP REM L11 (4 DUPLICATES REMOVED)

=> disp l12 ibib abs 1-3

L12  ANSWER 1 OF 3     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    97304299     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9160662
TITLE:               Polycythemia vera. V. Enhanced proliferation and
                     phosphorylation due to vanadate are diminished in
                     polycythemia vera erythroid progenitor cells: a
                     possible defect of phosphatase activity in polycythemia
                     vera.
AUTHOR:              Dai C H; Krantz S B; Sawyer S T
CORPORATE SOURCE:    Department of Medicine, Department of Veterans Affairs
                     Medical Center, Vanderbilt University School of Medicine,
                     Nashville, TN 37232-6305, USA.
SOURCE:              Blood, (1997 May 15) Vol. 89, No. 10, pp. 3574-81.
                     Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         199706
ENTRY DATE:          Entered STN: 30 Jun 1997
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Last Updated on STN: 3 Mar 2000
Entered Medline: 19 Jun 1997

AB Erythropoietin (EP) and stem cell factor (SCF) are essential growth factors for erythroid progenitor cell proliferation and differentiation in serum-free culture. It has been previously shown that burst-forming units-erythroid and colony-forming units-erythroid from patients with polycythemia vera (PV) have enhanced sensitivity to EP and SCF compared with normal erythroid progenitors, but little is known about the mechanism for this difference. In the present investigation, the effect of EP and SCF on protein tyrosine phosphorylation in day-8 normal and PV erythroid colony-forming cells, which give rise to colonies of 2-49 hemoglobinized cells, was studied. EP rapidly induced tyrosine phosphorylation of the EP receptor, whereas the most prominent phosphorylated protein induced by SCF was identified as the SCF receptor. No additional phosphorylated proteins were evident when PV cells were compared with normal cells. Culture of normal erythroid progenitors with orthovanadate, an inhibitor of protein tyrosine phosphatases, resulted in an increased number of erythroid colonies and enhanced protein tyrosine phosphorylation. However, in contrast, little enhancement was evident with PV cells. These results indicate that, although vanadate may be acting in normal erythroid progenitors as a phosphatase inhibitor that potentiates the kinase activity induced by SCF and EP, this function is diminished in PV cells. Because erythropoiesis is regulated by a balance between protein tyrosine kinase activity and protein tyrosine phosphatase activity, PV patients may have an abnormal phosphatase activity allowing increased cell proliferation.

L12 ANSWER 2 OF 3 MEDLINE on STN
ACCESSION NUMBER: 95143101 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7530982
TITLE: Effect of epidermal growth factor on cadherin-mediated adhesion in a human oesophageal cancer cell line.
AUTHOR: Shiozaki H; Kadowaki T; Doki Y; Inoue M; Tamura S; Oka H; Iwazawa T; Matsui S; Shimaya K; Takeichi M; +
CORPORATE SOURCE: Department of Surgery II, Osaka University Medical School, Japan.
SOURCE: British journal of cancer, (1995 Feb) Vol. 71, No. 2, pp. 250-8.
Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 16 Mar 1995
Last Updated on STN: 3 Mar 2000
Entered Medline: 9 Mar 1995

AB Epidermal growth factor (EGF) mediates many pleiotrophic biological effects, one of which is alteration of cellular morphology. In the present study, we examine the possibility that this alteration in cell morphology is caused in part by the dysfunction of cadherin-mediated cell-cell adhesion using the human oesophageal cancer cell line TE-2R, which expresses E-cadherin and EGF receptor. In the presence of EGF, TE-2R changed its shape from round to fibroblastic and its colony formation from compact to sparse. Vanadate, a tyrosine phosphatase inhibitor, further potentiated the EGF response, whereas herbimycin A, a tyrosine kinase inhibitor, interfered with it. Moreover, EGF enabled the cells to invade in organotypic raft culture. These phenomena were accompanied not by decreased expression of the E-cadherin molecule but by a change in its localisation from the lateral adhesion site to the whole cell surface. Both alpha- and

beta-catenin, cadherin-binding proteins, were also expressed at the same level throughout these morphological changes. Finally, we examined tyrosine phosphorylation of E-cadherin and alpha- and beta-catenin, and observed tyrosine phosphorylation of beta-catenin induced by EGF. These results suggest that EGF counteracts E-cadherin-mediated junctional assembly through phosphorylation of beta-catenin and modulates tumour cell behaviour to a more aggressive phenotype.

L12 ANSWER 3 OF 3 MEDLINE on STN
ACCESSION NUMBER: 95057973 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7968349
TITLE: Protein kinases mediate basic fibroblast growth factor's stimulation of proliferation and c-fos induction in oligodendrocyte progenitors.
AUTHOR: Radhakrishna M; Almazan G
CORPORATE SOURCE: Department of Pharmacology and Therapeutics, McGill University, Montreal, Que., Canada.
SOURCE: Brain research. Molecular brain research, (1994 Jul) Vol. 24, No. 1-4, pp. 118-28.
Journal code: 8908640. ISSN: 0169-328X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 10 Jan 1995
Last Updated on STN: 6 Feb 1998
Entered Medline: 7 Dec 1994

AB Primary culture was used to examine the effects of basic fibroblast growth factor (bFGF) on oligodendrocyte progenitor proliferation and c-fos expression. Basic FGF induced proliferation approximately six fold. This increased DNA synthesis could be blocked both with genistein, a tyrosine kinase inhibitor, and H-7, a protein kinase C (PKC) inhibitor. These results indicate that protein tyrosine kinase activity and protein kinase C are involved in mediating oligodendrocyte progenitor proliferation. The protooncogene c-fos was investigated as a likely proliferation mediator. Firstly, optimal conditions for bFGF-induced c-fos expression were determined. The oncogene responded maximally between 30 and 60 min of bFGF stimulation. Induction in response to bFGF occurred at 1 ng/ml, increased in a concentration-dependent manner and was maximal at 50 ng/ml. H-7 (50 microM) and genistein (100 microM) blocked c-fos induction as did PKC down-regulation with chronic treatment of phorbol 12-myristate 13-acetate. These results indicate that bFGF induces c-fos expression through receptor tyrosine phosphorylation and PKC activation. Thus similar early signals lead to bFGF-driven proliferation and c-fos induction suggesting a link between these two processes.

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FILE LAST UPDATED: 6 Dec 2007  (20071206/ED)

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=> S (E3) AND (VANADATE)
             7 "HAGGBLAD JOHAN"/IN
         24227 VANADATE
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                 (VANADATE OR VANADATES)
L1           1 ("HAGGBLAD JOHAN"/IN) AND (VANADATE)

=> DIS L1 1 IBIB IABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.83 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y
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L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:183009 CAPLUS
DOCUMENT NUMBER: 140:232116
TITLE: Culturing stem cells in the presence of vanadate and other phosphate mimics and possible therapeutic applications in the treatment of neurodegenerative disorders
INVENTOR(S): Haggblad, Johan; Horrocks, Carolyn; Jansson, Katarina; Ronnholm, Harriet
PATENT ASSIGNEE(S): Neuronova AB, Swed.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004018655	A2	20040304	WO 2003-IB4388		20030826
WO 2004018655	A3	20040902			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003265094	A1	20040311	AU 2003-265094		20030826
US 2006128014	A1	20060615	US 2005-525930		20050225
PRIORITY APPLN. INFO.:			US 2002-406688P	P	20020826
			WO 2003-IB4388	W	20030826

ABSTRACT:
The present invention provides methods of culturing, propagating, treating, and maintaining stem cells in the presence of a phosphate mimic, such as ***vanadates.*** The authors have discovered that a phosphate mimic, ***vanadate*** , when added to defined culture medium makes neural stem cells proliferate and form neurospheres in a fashion similar to treatment of the stem cells with protein growth factors (e.g., but not limited to EGF and FGF2). The mode of action of vanadate is most likely through inhibition of PTPases, thereby prolonging the action of insulin in the defined medium, and of growth factor release by the cells to the surrounding medium. The observed action of vanadate can be used in stem cell originating dysfunctions and diseases and as a tool to culture and maintain stem cells for the purpose of transplantation, drug screening and diagnosis of disease. In conclusion, ***vanadate*** can be added to culture medium devoid of growth factors except for the supplement component insulin and thereby by itself trigger proliferation and expansion of adult derived neural stem cells. The effect is additive to two other proliferative cues (growth factor or cAMP). This effect can be used in vitro for, e.g., cell culture purposes or in vivo for therapeutic purposes, such as the treatment of neurodegenerative disorders.

=> E HORROCKS CAROLYN/IN 25
E1 3 HORROCKS BRIAN J/IN
E2 1 HORROCKS BRIAN JOHN/IN
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E5 5 HORROCKS DONALD L/IN
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                 (VANADATE OR VANADATES)
L2           1 ("HORROCKS CAROLYN"/IN) AND (VANADATE)

=> DIS L2 1 IBIB IABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.83 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L2   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2004:183009  CAPLUS
DOCUMENT NUMBER:         140:232116
TITLE:                   Culturing stem cells in the presence of
                         vanadate and other phosphate mimics and
                         possible therapeutic applications in the treatment of
                         neurodegenerative disorders
INVENTOR(S):             Haggblad, Johan; Horrocks, Carolyn; Jansson,
                         Katarina; Ronnholm, Harriet
PATENT ASSIGNEE(S):      Neuronova AB, Swed.
SOURCE:                  PCT Int. Appl., 83 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     WO 2004018655         A2    20040304    WO 2003-IB4388           20030826
     WO 2004018655         A3    20040902
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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     AU 2003265094         A1    20040311    AU 2003-265094           20030826
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US 2006128014 A1 20060615 US 2005-525930 20050225
PRIORITY APPLN. INFO.: US 2002-406688P P 20020826
WO 2003-IB4388 W 20030826

ABSTRACT:
The present invention provides methods of culturing, propagating, treating, and maintaining stem cells in the presence of a phosphate mimic, such as ***vanadates.*** The authors have discovered that a phosphate mimic, ***vanadate*** , when added to defined culture medium makes neural stem cells proliferate and form neurospheres in a fashion similar to treatment of the stem cells with protein growth factors (e.g., but not limited to EGF and FGF2). The mode of action of vanadate is most likely through inhibition of PTPases, thereby prolonging the action of insulin in the defined medium, and of growth factor release by the cells to the surrounding medium. The observed action of vanadate can be used in stem cell originating dysfunctions and diseases and as a tool to culture and maintain stem cells for the purpose of transplantation, drug screening and diagnosis of disease. In conclusion, ***vanadate*** can be added to culture medium devoid of growth factors except for the supplement component insulin and thereby by itself trigger proliferation and expansion of adult derived neural stem cells. The effect is additive to two other proliferative cues (growth factor or cAMP). This effect can be used in vitro for, e.g., cell culture purposes or in vivo for therapeutic purposes, such as the treatment of neurodegenerative disorders.

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=> S (E3) AND (VANADATE)
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                 (VANADATE OR VANADATES)
L3           1 ("JANSSON KATARINA"/IN) AND (VANADATE)

=> DIS L3 1 IBIB IABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.83 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y
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L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:183009 CAPLUS
DOCUMENT NUMBER: 140:232116
TITLE: Culturing stem cells in the presence of vanadate and other phosphate mimics and possible therapeutic applications in the treatment of neurodegenerative disorders
INVENTOR(S): Haggblad, Johan; Horrocks, Carolyn; Jansson, Katarina; Ronnholm, Harriet
PATENT ASSIGNEE(S): Neuronova AB, Swed.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004018655	A2	20040304	WO 2003-IB4388		20030826
WO 2004018655	A3	20040902			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003265094	A1	20040311	AU 2003-265094		20030826
US 2006128014	A1	20060615	US 2005-525930		20050225
PRIORITY APPLN. INFO.:			US 2002-406688P	P	20020826
			WO 2003-IB4388	W	20030826

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=> DIS L3 1 IBIB IABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.83 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:183009 CAPLUS
DOCUMENT NUMBER: 140:232116

TITLE: Culturing stem cells in the presence of vanadate and other phosphate mimics and possible therapeutic applications in the treatment of neurodegenerative disorders

INVENTOR(S): Haggblad, Johan; Horrocks, Carolyn; Jansson, Katarina; Ronnholm, Harriet

PATENT ASSIGNEE(S): Neuronova AB, Swed.

SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004018655	A2	20040304	WO 2003-IB4388		20030826
WO 2004018655	A3	20040902			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003265094	A1	20040311	AU 2003-265094		20030826
US 2006128014	A1	20060615	US 2005-525930		20050225
PRIORITY APPLN. INFO.:			US 2002-406688P	P	20020826
			WO 2003-IB4388	W	20030826

ABSTRACT:
The present invention provides methods of culturing, propagating, treating, and maintaining stem cells in the presence of a phosphate mimic, such as ***vanadates.*** The authors have discovered that a phosphate mimic, ***vanadate*** , when added to defined culture medium makes neural stem cells proliferate and form neurospheres in a fashion similar to treatment of the stem cells with protein growth factors (e.g., but not limited to EGF and FGF2). The mode of action of vanadate is most likely through inhibition of PTPases, thereby prolonging the action of insulin in the defined medium, and of growth factor release by the cells to the surrounding medium. The observed action of vanadate can be used in stem cell originating dysfunctions and diseases and as a tool to culture and maintain stem cells for the purpose of transplantation, drug screening and diagnosis of disease. In conclusion, ***vanadate*** can be added to culture medium devoid of growth factors except for the supplement component insulin and thereby by itself trigger proliferation and expansion of adult derived neural stem cells. The effect is additive to two other proliferative cues (growth factor or cAMP). This effect can be used in vitro for, e.g., cell culture purposes or in vivo for therapeutic purposes, such as the treatment of neurodegenerative disorders.

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=> E RONNHOLM HARRIET/IN 25
E1            1     RONNHOLM ARVI A R/IN
E2            2     RONNHOLM ARVI AIOL RAFAEL/IN
E3           10 --> RONNHOLM HARRIET/IN
E4            2     RONNIE ABRAHAM ARAV/IN
E5            1     RONNIGER GISELA/IN
E6            2     RONNING ALBERT J/IN
E7            1     RONNING ERIC D/IN
E8            1     RONNING JAMES/IN
E9            1     RONNING JAMES A/IN
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E10          2      RONNING JEFFREY J/IN
E11          1      RONNING LENNART/IN
E12          1      RONNING MAGNUS/IN
E13          1      RONNING MICHAEL T/IN
E14          1      RONNING ODD/IN
E15          1      RONNING OYSTEIN/IN
E16          3      RONNING PATRICIA M/IN
E17          1      RONNING PER/IN
E18          1      RONNING POUL/IN
E19          1      RONNING RICHARD L/IN
E20          1      RONNING SANDRA HRUZA/IN
E21          2      RONNING STEPHANIE/IN
E22          1      RONNING TROND A/IN
E23          1      RONNING V C/IN
E24          1      RONNMARK KJELL O/IN
E25          1      RONNMARK PER MAGNUS LENNART/IN

=> S (E3) AND (VANADATE)
            10 "RONNHOLM HARRIET"/IN
         24227 VANADATE
          3518 VANADATES
         25486 VANADATE
                (VANADATE OR VANADATES)
L4           1 ("RONNHOLM HARRIET"/IN) AND (VANADATE)

=> DIS L4 1 IBIB IABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.83 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L4   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:183009  CAPLUS
DOCUMENT NUMBER:          140:232116
TITLE:                    Culturing stem cells in the presence of
                          vanadate and other phosphate mimics and
                          possible therapeutic applications in the treatment of
                          neurodegenerative disorders
INVENTOR(S):              Haggblad, Johan; Horrocks, Carolyn; Jansson, Katarina;
                          Ronnholm, Harriet
PATENT ASSIGNEE(S):       Neuronova AB, Swed.
SOURCE:                   PCT Int. Appl., 83 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

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     WO 2004018655         A2    20040304    WO 2003-IB4388           20030826
     WO 2004018655         A3    20040902
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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